

WHAT IS CLAIMED IS:

1. A method for constructing a normalized cDNA library of genes of low expression, comprising:

- 5 (a) constructing a non-normalized cDNA library from an RNA sample, wherein said RNA sample contains different species of RNA of different amounts, wherein said non-normalized cDNA library contains a plurality of members;
- (b) separating the members of said non-normalized cDNA library;
- (c) constructing a labeled probe library from said RNA sample;
- 10 (d) hybridizing a labeled probe library to said non-normalized cDNA library, whereby there is a differential of the amount of labeled probe of said labeled probe library hybridized to each individual member of said non-normalized cDNA library;
- (e) identifying the individual members of said non-normalized cDNA library hybridized with low amounts of labeled probe; and
- 15 (f) pooling the individual members of said non-normalized cDNA library identified in step (e) in a collection;
- whereby said collection is said normalized cDNA library of genes of low expression.

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2. The method according to Claim 1, wherein said RNA sample is obtained from a cell.

3. The method according to Claim 2, wherein said RNA sample is a mRNA sample.

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4. The method according to Claim 2, wherein said cell is an eubacteria, archaeobacteria, or eukaryotic cell.

5. The method according to Claim 4, wherein said eukaryotic cell is a plant cell or animal cell.

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6. The method according to Claim 5, wherein said plant cell is a soy, tobacco, wheat, rice, or corn cell.

7. The method according to Claim 5, wherein said animal cell is a human, ape, mouse, rat, cow, pig, horse, goat, sheep, dog, cat, chicken, zebrafish, or fruitfly cell.

8. The method according to Claim 7, wherein said human cell is a human kidney cell.

9. The method according to Claim 1, wherein said normalized cDNA library is a normalized full-length cDNA library.

10. The method according to Claim 1, wherein said constructing comprises catalyzing a reverse transcription reaction for each species of said RNA sample, wherein said catalyzing takes place under conditions permissible for catalyzing a reverse transcription reaction.

11. The method according to Claim 10, wherein said catalyzing comprises:

- (i) hybridizing poly-T oligonucleotide primers to said RNA sample;
- (ii) adding dATP, dCTP, dGTP, dTTP, and reverse transcriptase; and
- (iii) incubating said RNA sample at a temperature permissible for catalyzing a reverse transcription reaction.

12. The method according to Claim 1, wherein said non-normalized cDNA library is a non-normalized full-length cDNA library.

13. The method according to Claim 1, further comprising:
transforming each member of said non-normalized cDNA library into a host cell, wherein said transforming step is subsequent to said constructing and prior to said hybridizing.

14. The method according to Claim 13, further comprising:
amplifying each member of said non-normalized cDNA library,
wherein said amplifying comprises growing each said host cell containing,
wherein said amplifying step is subsequent to said transforming and prior to said
5 hybridizing.
15. A method for constructing a normalized cDNA library, comprising:
- (a) constructing a non-normalized cDNA library from an RNA sample,
wherein said RNA sample contains different species of RNA of
10 different amounts, wherein each member of said non-normalized
cDNA library is separate from other members;
- (b) identifying the relative amounts of each member of said non-
normalized cDNA library represented in said RNA sample;
- (c) dividing the members of said non-normalized cDNA library into
15 groups; wherein one group of members of said non-normalized cDNA
library is represented in low amounts by said RNA sample and one or
more groups of members of said non-normalized cDNA library is
represented in high amounts by said RNA sample;
- (d) selecting one group of said one or more groups of members of said
20 non-normalized cDNA library represented in high amounts by said
RNA sample;
- (e) identifying the members in said group of members that is not
represented within a sub-group of members selected from said group of
members;
- (f) forming a group of members from the members identified in step (e)
25 and repeating step (e) until every member of said group of members
has been selected within a sub-group of members;
- (g) repeating steps (d)-(f) with every group of said one or more groups of
members of said non-normalized cDNA library represented in high
30 amounts by said RNA sample;

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- (h) pooling the members of said group of members of said non-normalized cDNA library represented in low amounts by said RNA sample and the members of every sub-group selected in a collection; whereby said collection is said normalized cDNA library.

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16. The method according to Claim 15, wherein said RNA sample is obtained from a cell.

17. The method according to Claim 16, wherein said RNA sample is a mRNA sample.

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18. The method according to Claim 16, wherein said cell is an eubacteria, archaeobacteria, or eukaryotic cell.

19. The method according to Claim 18, wherein said eukaryotic cell is a plant cell or animal cell.

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20. The method according to Claim 19, wherein said plant cell is a soy, tobacco, wheat, rice, or corn cell.

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21. The method according to Claim 19, wherein said animal cell is a human, ape, mouse, rat, cow, pig, horse, goat, sheep, dog, cat, chicken, zebrafish, or fruitfly cell.

22. The method according to Claim 21, wherein said human cell is a human kidney cell.

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23. The method according to Claim 15, wherein said normalized cDNA library is a normalized full-length cDNA library.

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24. The method according to Claim 15, wherein said constructing comprises catalyzing a reverse transcription reaction for each species of said RNA

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sample, wherein said catalyzing takes place under conditions permissible for catalyzing a reverse transcription reaction.

- 5 25. The method according to Claim 24, wherein said catalyzing comprises:
- (i) hybridizing poly-T oligonucleotide primers to said RNA sample;
 - (ii) adding dATP, dCTP, dGTP, dTTP, and reverse transcriptase; and
 - (iii) incubating said RNA sample at a temperature permissible for catalyzing a reverse transcription reaction.

- 10 26. The method according to Claim 15, wherein said non-normalized cDNA library is a non-normalized full-length cDNA library.

- 15 27. The method according to Claim 15, further comprising:
transforming each member of said non-normalized cDNA library into a host cell, wherein said transforming step is subsequent to said constructing and prior to said identifying of step (b).

- 20 28. The method according to Claim 27, further comprising:
amplifying each member of said non-normalized cDNA library,
wherein said amplifying comprises growing each said host cell containing,
wherein said amplifying step is subsequent to said transforming and prior to said identifying of step (b).

- 25 29. The method according to Claim 15, wherein said identifying of step (b) comprises:
- (i) constructing a labeled probe library from said RNA sample;
 - (ii) hybridizing said labeled probe library to said non-normalized cDNA library;
 - (iii) identifying the relative amounts of labeled probe hybridized to each
- 30 member of said non-normalized cDNA library.

30. The method according to Claim 15, wherein said identifying of step (e) comprises:

- (i) constructing a labeled probe library from said sub-group of members;
- (ii) hybridizing said labeled probe library to said group of members;
- 5 (iii) identifying each member of said group of members that is not hybridized to by said labeled probe library.

31. The method according to Claim 15, further comprising:
sequencing every member of said group members of said non-normalized
10 cDNA library represented in low amounts by said RNA sample and every member of every sub-group selected prior to said pooling, wherein a sufficient number of nucleotides are sequenced to identify members that are represented by more than once; and
pooling every unique member determined by said sequencing.

32. A method for constructing a normalized cDNA library of genes of low expression, comprising:

- (a) constructing a non-normalized cDNA library from an RNA sample, wherein said RNA sample contains different species of RNA of different amounts, wherein each member of said non-normalized cDNA library is separate from other members;
- (b) identifying the relative amounts of each member of said non-normalized cDNA library represented in said RNA sample;
- (c) pooling the members of said group of members of said non-normalized cDNA library represented in low amounts by said RNA sample in a
25 collection;

whereby said collection is said normalized cDNA library of genes of low expression.

30 33. A normalized cDNA library generated by the method of Claim 1.

34. A normalized cDNA library generated by the method of Claim 8.

35. A normalized cDNA library generated by the method of Claim 15.

36. A normalized cDNA library generated by the method of Claim 32.

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